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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/797,462	03/10/2004	Lyle Brostrom	3300/8	4454

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EXAMINER

ZUCKER, PAUL A

ART UNIT PAPER NUMBER

1621

DATE MAILED: 08/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/797,462

Applicant(s)

BROSTROM ET AL.

Examiner

Paul A. Zucker

Art Unit

1621

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 12-15 is/are rejected.
- 7) ☒ Claim(s) 8-11 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 March 2004 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 6/14/2004.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION

Drawings

1. Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

Specification

2. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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3. Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 5 recites the limitation "a condition wherein pathologically high production forms a part" in line 1 but does not set forth that material whose production is pathologically high. It is therefore impossible to determine the intended scope of claim 5 which is therefore rendered indefinite.
4. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 15 recites "the ratio of anti-solvent" and the "ratio of solvent" in lines 1-2. It is unclear what relative amounts of materials these ratios define. Claim 15 is therefore rendered indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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5. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Webber et al (US 6,403,830 06-2002).

Instantly claimed are a crystalline form of S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine maleate hydrochloride and pharmaceutical formulations thereof.

Webber teaches (Column 64, lines 30-46) a method for the preparation of mixed salts from S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine maleate hydrochloride via the addition of a stoichiometric amount of the reagent diacid (R) to S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine dihydrochloride salt. The Examiner presumes that product crystallizes out upon addition of counter-ion producing acid since no further operation other than addition of acid is set forth by Webber. Webber exemplifies (Column 69-70, Table 4) the reaction of succinic acid. Webber teaches (Column 5, line 19- column 7, line 45) the treatment of a large number of conditions using the compounds of the invention. Webber teaches (Column 25, line 29- column 26, line 42) formulations containing these compounds as well.

The difference between the instantly claimed compounds and methods and those taught by Webber is that Webber exemplifies the formation of the S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine succinate hydrochloride and the S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine maleate hydrochloride is instantly claimed.

Webber, however, teaches (Column 80, lines 47-65, claim 8) the equivalence and, therefore, the interchangeability of the succinate and maleate salts. One of ordinary skill in the art would therefore have been motivated by Webber's teaching to make the instantly employed S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine maleate hydrochloride by the expectation that it would have similar properties to the S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine succinate hydrochloride exemplified by Webber. The instantly claimed crystalline properties (agglomerates) would be an inherent feature of the material so produced. In particular, the Examiner notes the claimed loss in mass on heating is consistent with loss of water from the crystals. There would have been a reasonable expectation for success based upon Webber's teaching (See above) of the equivalence of the succinate and maleate salts.

Thus the instantly claimed compounds, compositions and methods would have been obvious to one of ordinary skill in the art.

6. Claims 6, 7 and 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Webber et al (US 6,403,830 06-2002 as applied to claims 1-6 above, and further in view of McMasters (Chem2O06 Laboratory 1997, Expt. 1, Part B. Recrystallization and Melting Point Determinations. from world wide web :chemistry.mcmaster.ca/~chem2o6/labmanual/microscale/ms-recrs.html).

Instantly claimed are a crystalline form of S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine maleate hydrochloride and a method for its production.

The difference between the instantly claimed process and that taught by Webber is that Webber only teaches the method for the formation of S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine maleate hydrochloride and does not teach the method for purification by recrystallization of the material obtained.

McMasters, however, teaches (Page 1, 1st full paragraph and page 2, 1st and 2nd full paragraphs) recrystallization using a solvent/anti-solvent pair to create a two-phase (cloudy) solution for crystallization. McMasters further teaches (Page 2, last paragraph) the use of seed crystals. The determination of the amount of seed crystals to employ is well within the ambit of the ordinary artisan. The Examiner notes that alteration of the rate of super-saturation generation (e.g. controlling the rate of cooling) is standard crystallization practice.

Thus one of ordinary skill in the art wishing to purify the crystalline S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine maleate hydrochloride of Webber would have been motivated to employed the methods of McMasters since Webber does not provide any. Because of the generality of McMasters' teaching, there would have been a reasonable expectation for success.

Thus the instantly claimed methods would have been obvious to one of ordinary skill in the art.

Claim Objections

7. Claims 8-11 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Allowable Subject Matter

8. Claims 8-11 are drawn to allowable subject matter. The following is a statement of reasons for the indication of allowable subject matter: The instantly claimed solvents and anti-solvents are neither disclosed nor fairly suggested by the closest prior art : Webber et al (US 6,403,830 06-2002) and McMasters (Chem2006 Laboratory 1997, Expt. 1, Part B. Recrystallization and Melting Point Determinations. from world wide web :chemistry.mcmaster.ca/~chem2o6/labmanual/microscale/ms-recrs.html).


Conclusion

9. Claims 1-15 are pending. Claims 1-7 and 12-15 are rejected. Claims 8-11 are objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul A. Zucker whose telephone number is 571-272-0650. The examiner can normally be reached on Monday-Friday 5:30-2:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



PAULA A. ZUCKER, PH.D.
PRIMARY EXAMINER

